



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

Address: COMMISSIONER FOR PATENTS

P.O. Box 1450

Alexandria, Virginia 22313-1450

www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,013	03/16/2004	Bruce F. Molino	20011/1331	4932

7590
Michael L. Goldman
Nixon Peabody LLP
Clinton Square
P.O. Box 31051
Rochester, NY 14603-1051

07/14/2008

EXAMINER

CORDERO GARCIA, MARCELA M

ART UNIT

PAPER NUMBER

1654

MAIL DATE

DELIVERY MODE

07/14/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/802,013

Applicant(s)

MOLINO ET AL.

ExaminerMARCELA M. CORDERO
GARCIA**Art Unit**

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04/17/2008.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-103 is/are pending in the application.
4a) Of the above claim(s) 4-12, 14, 16-39 and 47-188 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1 and 103 is/are rejected.
7) ☒ Claim(s) 2-3 is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 04/08
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 17 April 2007 has been entered.

Claims 1-12, 14, 16-39, 47-188 are pending in the application. Claims 4-12, 14, 16-39, 47-188 are withdrawn as not drawn to the elected Group or the elected and examined species.

Applicant originally elected with traverse Group I, drawn to cyclosporine compounds, claims 1-103. The species elected by Applicant was a compound of Formula (I) wherein A is an amino acid of Formula (II) and wherein R₀ is CH₃; R₁ is CH=CHC(=O)Me; X is hydroxyl; B is aminobutyric acid; C is a sarcosine; D is N-methyl leucine; E is valine; F is an N-methyl leucine; G is alanine; H is D-alanine; I is N-methyl leucine; J is N-methyl leucine; and K is N-methyl valine, with claims 1-3 readable thereon. Applicant's elected species was searched and found free of the prior art. Claim 3 is drawn exclusively to this species and would be allowable if written in independent form.

The search was broadened by Examiner, namely, a compound of Formula (I) wherein A is an amino acid of Formula (II) and wherein R₀ is CH₃; R₁ is CR₁₃R₁₄R₁₅ with

Art Unit: 1654

$R_{13} = R_{14} = H$ and $R_{15} =$ substituted and unsubstituted C_2-C_6 -straight alkenyl chain; X is hydroxyl; B is α -aminobutyric acid; C is a sarcosine; D is N-methyl-leucine; E is valine; F is an N-methyl leucine; G is alanine; H is D-alanine; I is N-methyl leucine; J is N-methyl leucine; and K is N-methyl valine. The 102(b) and ODP rejections presented were withdrawn based on Applicant's amendments.

Examiner's new matter rejection over claims 1-103 has now been overcome by Applicant's amendments deleting the proviso previously presented. Examiner's previous written description rejection has been withdrawn based on the evidence presented in the 37 CFR 1.132 Affidavit filed 17 April 2008 which presents immunosuppressive activity for selected compounds and controls (see Table 2) is deemed sufficient to overcome the written description rejection of record.

Examiner has broadened the search and a species was found. Claims 1-3 and 103 are presented for examination on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 103 are rejected under 35 U.S.C. 102(b) as being anticipated by Witzel (US 4,798,823).

Witzel teaches a compound of Formula 1 wherein A is an amino acid of Formula II with $R_0 = H$, $X = OH$, R_a is CH_3 (Example 2) and R_1 is CH_2S -alkyl-thio-lower alkyl (see

Art Unit: 1654

claim 1, see also column 3, lines 62-65) which reads upon $R_1 = \text{CH}(\text{SR}_{12})_2$ wherein R_{12} is $\text{C}_1\text{-C}_6$ —straight alkyl chain, B is Abu, C is Sar, D is MeLeu, E is Val, F is MeLeu, G is Ala, H is D-Ala, I is MeLeu, J is MeLeu, K is MeVal. The limitation of claim 103: "pharmaceutical composition" is taught, e.g., in column 2, lines 42-46.

Therefore the reference is deemed to anticipate the instant claim above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 and 103 rejected under 35 U.S.C. 103(a) as being unpatentable over Witzel (US 4,798,823).

Witzel teaches a compound of Formula 1 wherein A is an amino acid of Formula II with $R_0 = \text{H}$, $X = \text{OH}$, R_a is CH_3 (Example 2) and R_1 is $\text{CH}_2\text{S-alkyl-thio-lower alkyl}$ (see claim 1, see also column 3, lines 62-65) which reads upon $R_1 = \text{CH}(\text{SR}_{12})_2$ wherein R_{12} is $\text{C}_1\text{-C}_6$ —straight alkyl chain, B is Abu, C is Sar, D is MeLeu, E is Val, F is MeLeu, G is Ala, H is D-Ala, I is MeLeu, J is MeLeu, K is MeVal. Witzel teaches compounds encompassed by claim 1 which are analogs with immunosuppressive activity and ability to restore the balance of the help-and-suppression mechanism of the immune system by acting at an earlier point that the anti-inflammatory agents and (2) induce specific long-term transplantation tolerance through a suppressor cell circuit without increasing

Art Unit: 1654

the body's susceptibility to infection (e.g., column 2, lines 34-45) without the nephrotoxic side effects of cyclosporine (e.g., column 2, lines 20-33).

Witzel does not expressly teach the compounds of Example 2 wherein the amino acid A has $R_1 = CH(SR_{12})_2$, however, claim 1 and column 3, lines 62-65 describe such substitutions.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the compositions of Witzel (as in Example 2) as taught also by Witzel in claim 1 and column 3, lines 62-65. The skilled artisan would have been motivated to do given that such substitutions were taught to produce less toxic (e.g., column 2, lines 20-33) cyclosporine analogs with immunosuppressive activity and ability to restore the balance of the help-and-suppression mechanism of the immune system by acting at an earlier point than the anti-inflammatory agents and (2) induce specific long-term transplantation tolerance through a suppressor cell circuit without increasing the body's susceptibility to infection (e.g., column 2, lines 34-45). There would have been a reasonable expectation of success, to do so because the general formula of Example 2 is encompassed within the broader genus of claim 1 of Witzel. Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claim Objections

Claims 2-3 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Art Unit: 1654

Conclusion

No claim is allowed. Claims 2-3 are objected. Claims 1 and 103 are rejected.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCELA M. CORDERO GARCIA whose telephone number is (571)272-2939. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marcela M Cordero Garcia/
Patent Examiner, Art Unit 1654

07/08 MMCG

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654